K123905

JAN 14 2013

3. 510(k) Summary

The CDC hereby submits this special 510(k) in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

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Proprietary Name
CDC Human Influenza Virus Real-time RT-PCR Diagnostic Panel

Common or Usual Name

Human Influenza Virus Real-time RT-PCR Diagnostic Panel

Regulatory Information
Classification Regulation Section: 866.3332- Reagents for detection of specific novel influenza A viruses
Subsequent Regulation Sections: 866.3980- Respiratory viral panel multiplex nucleic acid assay
862.2570- Instrumentation for clinical multiplex test systems
Classification: Class II
Classification Product Code: OQW
Subsequent Product Codes: NSU, NXD, OEP
Panel: Microbiology

Predicate Device
CDC Human Influenza Virus Real-time RT-PCR Diagnostic Panel (K111507)

Device Description
The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel is used in real-time RT-PCR (rRT-PCR) assays on the ABI 7500 Fast Dx Real-Time PCR Instrument. The panel consists of oligonucleotide primers and dual-labeled hydrolysis (TaqMan®) probes to be used in rRT-PCR for the in vitro qualitative detection and characterization of human influenza viruses from viral RNA in respiratory specimens from patients presenting with influenza-like illness (ILI).

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel is based on technology which is used in many molecular diagnostic assays. rRT-PCR assays are one-tube assays that first reverse-transcribe specific regions of RNA into cDNA copies. The cDNA then serves as a template for a polymerase chain reaction that utilizes a thermocyclic heating and cooling of the reaction to logarithmically amplify a specific region of DNA. The probe anneals to a specific internal target sequence located between the target loci of the forward and reverse primers. During the extension phase of the PCR cycle, the 5' nuclease activity of Taq polymerase degrades any probe molecules hybridized to amplified target sequence, causing the reporter dye to separate from the quencher dye, and generating a fluorescent signal. With each cycle, additional reporter dye molecules are cleaved from their respective probes, increasing the fluorescence intensity. Fluorescence intensity is monitored at each PCR cycle. Amplification of targets is reflected by logarithmic increase in fluorescence over time in comparison to the background signal.

Intended Use

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel is intended for use in rRT-PCR assays on an ABI 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information:

- For qualitative detection of influenza virus type A or B viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) and lower respiratory tract specimens (including bronchoalveolar lavage [BAL], bronchial wash [BW], tracheal aspirate [TA], sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture.

- For determination of the subtype of seasonal human influenza A virus as seasonal A/H1, A/H3, and/or A/H1pdm09 from viral RNA in upper respiratory tract clinical specimens (including NPS, NS, TS, NA, NW, and NPS/TS) and lower respiratory tract specimens (including BAL, BW, TA, sputum and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture.

- For the presumptive identification of virus in patients who may be infected with influenza A subtype A/H5 (Asian Lineage) from viral RNA in human respiratory specimens and viral culture in conjunction with clinical and epidemiological risk factors.

- To provide epidemiologic information for surveillance of circulating influenza viruses.

Performance characteristics for influenza were established during a season when seasonal influenza viruses A/H1 and A/H3 were the predominant influenza A viruses in circulation and during a season when the A/H1pdm09 influenza virus was the predominant influenza A virus in circulation. Performance characteristics may vary with other emerging influenza A viruses.

Testing with the influenza H5a and H5b primer and probe sets should not be performed unless the patient meets the most current U.S. Department of Health and Human Services (DHHS) clinical and epidemiologic criteria for testing suspect A/H5 specimens. The definitive identification of influenza A/H5 (Asian lineage) either directly from patient specimens or from virus cultures requires additional

laboratory testing, along with clinical and epidemiological assessment in consultation with national influenza surveillance experts.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other patient management decisions. Conversely, positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease.

If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted unless a BSL 3+ facility is available to receive and culture specimens.

All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.

Indications for Use

The CDC Human Influenza Virus Real-Time PCR Diagnostic Panel is intended for use in Real-time RT-PCR assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument in conjunction with clinical and epidemiological information:

- For qualitative detection of influenza virus type A or B from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes and dual nasopharyngeal/throat swabs), and lower respiratory tract specimens (including bronchoalveolar lavages, bronchial washes, tracheal aspirates, sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture
- For determination of the subtype of seasonal human influenza A virus as seasonal A/H1, A/H3, and/or A/H1pdm09 from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes and dual nasopharyngeal/throat swabs), and lower respiratory tract specimens (including bronchoalveolar lavages, bronchial washes, tracheal aspirates, sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture
- For the presumptive identification of virus in patients who may be infected with influenza A subtype A/H5(Asian Lineage) from viral RNA in human respiratory specimens and viral culture in conjunction with clinical and epidemiological risk factors, and 4) to provide epidemiologic information for surveillance of the circulating influenza viruses

Technological Characteristics

The change proposed to the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel subject to this special 510(k) will not alter the device's design or technological attributes.

Substantial Equivalence Comparison

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel (K111507) will serve as the predicate for the intended change. Please see Table 1 for a detailed comparison.

Table 1: Device Comparison

	CDC Human Influenza Virus Real-time PCR Diagnostic Panel (K111507)	*Modified* CDC Human Influenza Virus Real-time PCR Diagnostic Panel
Intended Use	The CDC Human Influenza Virus Real-Time PCR Diagnostic Panel is intended for use in Real-time RT-PCR assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument in conjunction with clinical and epidemiological information: • for qualitative detection of influenza virus type A or B from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes and dual nasopharyngeal/throat swabs), and lower respiratory tract specimens (including bronchoalveolar lavages, bronchial washes, tracheal aspirates, sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture • for determination of the subtype of seasonal human influenza A virus as seasonal A/H1, A/H3, and/or A/H1pdm09 from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes and dual nasopharyngeal/throat swabs), and lower respiratory tract specimens (including bronchoalveolar lavages, bronchial washes, tracheal aspirates, sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture • for the presumptive identification of virus in patients who may be infected with influenza A subtype A/H5(Asian Lineage) from viral RNA in human respiratory specimens and viral culture in conjunction with clinical and epidemiological risk factors • to provide epidemiologic information for surveillance of the circulating influenza viruses.	Same

Specimen Types	Nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes and dual nasopharyngeal/throat swabs, bronchoalveolar lavages, bronchial aspirates, bronchial washes, tracheal aspirates, sputum, and lung tissue and virus culture.	Same
	CDC Human Influenza Virus Real-time PCR Diagnostic Panel (K111507)	**Modified CDC Human Influenza Virus Real-time PCR Diagnostic Panel**
Technology	Real-time RT-PCR	Same
Required Instrumentation	Applied Biosystems 7500 Fast Dx Real- Time PCR Instrument	Same
Organism Detected	Universal influenza A viruses (animal and human), Swine-origin influenza A viruses, Influenza B viruses, and Influenza A subtypes: seasonal A/H1, A/H3, A/H1pdm09 , and A/H5	Same
Nucleic Acid Extraction	Yes	Same
Extraction Method	• QIAamp® Viral RNA Mini Kit, Qiagen Inc. • MagNA Pure Compact -Total Nucleic Acid Kit, Roche Applied Science • MagNA Pure Compact – RNA Isolation Kit, Roche Applied Science • MagNA Pure LC - RNA Isolation Kit II, Roche Applied Science • Qiagen QIAcube with QIAamp® Viral RNA Mini Kit, Qiagen Inc. • NucliSENS® easyMAG®, bioMerieux	Same
Enzyme Master Mix	Invitrogen SuperScript™ III Platinum® One-Step Quantitative RT-PCR Kits (with or without ROX)	Same
Non Standard Results Guidance	Results positive for InfA, H3, and pdmInfA markers and negative for H1 and pdmH1 markers are reported as inconclusive and referred to CDC for further testing.	Results positive for InfA, H3, and pdmInfA markers and negative for H1 and pdmH1 markers are interpreted as a presumptive positive for influenza A (H3N2) variant virus and referred to CDC for further testing.

Performance Summary

Analytical Sensitivity – Limit of Detection (LOD)

The analytical sensitivity of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel for influenza A(H3N2) variant ((H3N2)v) virus was evaluated with two recent isolates by determining the lowest concentration of virus as measured by 50% egg infectious dose (EID_{50}/ml) where the InfA, pdmInfA, and H3 primer and probe sets demonstrated a uniform detection rate of ≥ 95%. The results are summarized in Table 2.

Table 2: (H3N2)v LOD Summary

Influenza A(H3N2)v virus	Limit of Detection (EID_{50}/mL)			
	InfA	pdm InfA	H3	Final LOD
A/West Virginia/06/2011	$10^{0.7}$	$10^{1.4}$	$10^{2.1}$	$10^{2.1}$

A/Indiana/12/2012	$10^{0.6}$	$10^{1.3}$	$10^{2.0}$	$10^{2.0}$

Analytical Sensitivity – Inclusivity

Recent isolates of influenza A(H3N2)v virus from 2009- 2012 were evaluated with the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel at virus concentrations of approximately $10^{2.0}$ EID_{50}/ml. The inclusivity testing verifies that the device can detect contemporary influenza A (H3N2)v viruses near the LOD. The results are summarized in Table 3.

Table 3: Inclusivity Testing

Strain designation	EID_{50}/mL	Average InfA Ct Value (n=3)	Average pdm InfA Ct Value (n=3)	Average H3 Ct Value (n=3)
A/Kansas/13/2009	$10^{2.0}$	33.4	32.6	33.9
A/Indiana/08/2011	$10^{2.3}$	33.0	33.5	35.6
A/Wisconsin/12/2011	$10^{2.1}$	28.9	26.9	28.9
A/West Virginia/06/2011	$10^{2.9}$	28.1	28.3	30.1
A/Indiana/12/2012	$10^{2.1}$	31.7	32.8	36.0

Clinical Specimen Testing

From July 2012-August 2012, a total of 165 human respiratory specimens that tested positive for InfA, H3, and pdmInfA markers and negative for H1 and pdmH1 markers with the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel were transferred from U.S. public health laboratories to the CDC for confirmatory testing.

The specimens were retested upon arrival with the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel following the instructions for use provided in the package insert. Results were confirmed through genetic sequence analysis. Comparison of the results obtained with the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel to the results of the genetic sequencing analysis demonstrate a positive percent agreement of 97.6% with a 95% confidence interval of 93.9-99.1 % for the detection of influenza A(H3N2)v virus.

Table 4: Clinical Performance Comparison

	Comparator[1]		
	Positive[2]	Negative	Performance
CDC Flu rRT-PCR Dx Panel (+)	161	NA	97.6% Positive Percent Agreement (93.9 – 99.1) 95% CI
CDC Flu rRT-PCR Dx Panel (-)	4	NA	NA
Total	165	NA	NA

[1]The comparator is genetic sequence analysis.

[2]A positive result for InfA, H3, and pdmInfA markers (negative for H1 and pdmH1 markers) was investigated. Any result that was not positive for all three markers InfA, pdm InfA, and H3 was considered negative.

NA = not applicable.

Risk Analysis

The risk analysis for the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel was reviewed to verify that the change did not present increased or new risks to the user. No new risks were identified as a result of the proposed modification. As an additional mitigation, specimens containing influenza A (H3N2)v viruses will continue to be referred immediately to the CDC for further confirmation.

Substantial Equivalence Conclusion

The changes proposed to the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel do not alter the device's design or technological attributes. In addition, the indications for use and intended use of the device will remain the same. It is only the interpretation of the results that will be modified, allowing users to report the result as a presumptive positive for influenza A (H3N2) variant virus instead of inconclusive. This information, along with the results of the performance testing, demonstrates that the modified device is substantially equivalent to the predicate.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

JAN 14 2013

Centers for Disease Control and Prevention
c/o Hye-Joo Kim, Pharm.D.
Associate Director for Regulatory Affairs
Office of the Director, National Center for Emerging and Zoonotic Infectious Diseases
1600 Clifton Road, MS-C18
Atlanta, GA 30333

Re: k123905
Trade/Device Name: CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel
Regulation Number: 21 CFR 866.3332
Regulation Name: Reagents for Detection of Specific Novel Influenza A Viruses
Regulatory Class: Class II
Product Code: OQW, NSU, NXD, OEP
Dated: December 18, 2012
Received: December 19, 2012

Dear Captain Kim:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set

forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostics and Radiological Health at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

2. Indications for Use Statement

510(k) Number (if known): k123905

Device Name: **CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel**

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Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of *In Vitro* Diagnostics and Radiological Health (OIR)

Division Sign-Off
Office of *In Vitro* Diagnostics and Radiological Health

Tamara P. Feldblum

Division Sign-Off

Office of In Vitro Diagnostics and Radiological Health

510(k) K123905